REMARKS

The Office action mailed 14 February 2003, has been received and its contents carefully noted. Claims 1-11 were pending and claims 8-11 were rejected. By this amendment, claims 1, 8, and 9 have been amended. Claim 1 was amended to address nonsubstantive informalities. Claim 8 was amended to include a step that accomplishes the purpose stated in the preamble of the claim. Claim 9 was amended to include instructions for performing the method of claim 1. Support may be found throughout the specification. New claims 12-16 have been added. Specific support may be found on page 7, lines 15-21 and the Examples. No statutory new matter has been added. Reconsideration is respectfully requested.

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejected claim 8 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting steps.

In a telephone interview with the Examiner on 7 May 2003, the Examiner indicated that amended claim 8 by adding "whereby an increased level indicates an increase in the breast cancer and a decreased level indicates a decrease in the breast cancer" would be sufficient to overcome the rejection. Applicants greatly appreciate the Examiner's assistance and have amended claim 8 as agreed. Therefore, the rejection under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

Rejection under 35 U.S.C. 102(b)

The Examiner rejected claims 9 and 10 under 35 U.S.C. 102(b) as being anticipated by Reilly *et al.* Specifically, the Examiner deemed that claims 9 and 10 are drawn to a kit whose main component is an antibody that specifically binds bFGF and that Reilly *et al.* teaches such an antibody.

Applicants respectfully submit that claims 9 and 10 as amended are not anticipated by Reilly *et al.* Specifically, claims 9 and 10 have been amended to include instructions for performing the method of claim 1. Nowhere do Reilly *et al.* teach or suggest the method of claim 1 or include instructions or other printed matter that teaches or suggests the method of claim 1. Therefore, Reilly *et al.* do not anticipate claims 8 and 9 and the rejection under 35 U.S.C. 102(b) should properly be withdrawn.

Rejection under 35 U.S.C. 103(a)

The Examiner rejected claim 11 under 35 U.S.C. 103(a) as being unpatentable over Reilly *et al.* as applied to claims 9 and 10 and further in view of the Sigma Catalog. Specifically, the Examiner deemed that the Sigma Catalog teaches that various protein inhibitors are known and sold for preserving proteins.

Applicants respectfully submit that the kit claims as amended and the new kit claims include the limitation that the kits include instructions for performing the method of claim 1 or claim 8. Applicants acknowledge that kits containing known compositions and instructions for performing known methods are obvious.

However, Applicants respectfully submit that kits containing known compositions and instructions for performing novel methods are nonobvious. *See In re Miller*, 418 F.2d 1392-1396 (printed matter should be given patentable weight when a novel relationship exists between the printed matter and the article); and *In re Gulack* 703 F.2d 1381-1388 (claims were patentable where there was a new and unobvious functional relationship between the printed matter and the article).

Applicants respectfully submit that the kit claims, claims 9-14, contain known reagents and instructions for performing the method of either claim 1 or claim 8. A novel and unobvious functional relationship exists between the instructions (printed matter) and the reagents, i.e. the ability to use the reagents to perform the novel and nonobvious method of claim 1 or claim 8. Therefore, Applicants respectfully submit that the inclusion of such instructions should be given patentable weight and accordingly that the rejection under 35 U.S.C. 103(a) be properly withdrawn.

Additionally, Applicants respectfully submit that the Patent Resources Group, Inc. course materials for the course entitled "Biotechnology: Patents, Licensing & FDA Practice" (2001) teach that claims to a kit or article of manufacture containing a known composition and printed material for its use in a new method may be patentable. See coursebook, page I-90 (enclosed).

Further, Applicants respectfully submit that the United States Patent and Trademark Office routinely issues claims to kits containing known compositions and instructions for

performing novel methods. See, for example, U.S. Patent No. 6,518,252 ('252 patent), issued 11 February 2003, entitled "Method of treating aquatic animals with an antimicrobial agent and chelating agent". Claim 1 of the '252 patent is a novel method claim and reads as follows:

> 1. A method for administering an antimicrobial composition to an aquatic animal to inhibit the proliferation of a microbial infection or colonization, comprising the steps of:
>
> a) dissolving an antimicrobial composition in a carrier to give an antimicrobial solution, wherein the antimicrobial composition comprises at least one chelating agent and at least one antibiotic;
>
> b) immersing an aquatic animal in the antimicrobial solution;
>
> c) removing an aquatic animal from the antimicrobial solution; and
>
> d) placing an aquatic animal in water not containing the antimicrobial composition.

Claim 34, of the '252 patent is a kit claim and reads as follows:

> 34. A kit for use in administering an antibiotic to an aquatic animal for inhibiting the proliferation of a microbial infection of the animal, comprising:
>
> at least one container having therein at least one chelating agent, and optionally at least one antibiotic; and packaging material, wherein the packaging material comprises instructions directing the use of the kit for administering the antibiotic and chelating agent to inhibit the proliferation of a microbial infection of an aquatic animal.

Applicants respectfully direct the Examiner's attention to the fact that chelating agents, antibiotics, and packaging material are known in the prior art. What is not known in the prior art is how to use the kit for administering the antibiotic and chelating agent to inhibit the proliferation of a microbial infection of an aquatic animal, i.e. the method of claim 1.

A second example is U.S. Patent No. 6,461,827 ('827 patent), issued 8 October 2002, entitled "Methods and kits for detecting or predicting ischemic disorders". Claim 1 is a method claim and reads as follows:

> 1. A method for detecting or predicting an ischemic disorder in a subject, the method comprising the following steps:
>
> (a) providing a first and a second body fluid sample, wherein the first sample is

taken from a test subject from which an ischemic disorder is to be detected or predicted and the second sample is taken from a normal subject, and the body fluid sample is selected from the group consisting of a blood sample, a urine sample, a saliva sample and a semen sample;

(b) providing a first antibody and a second labeled antibody, wherein both the first and the second antibodies are capable of specifically binding to a human lipocalin-type prostaglandin D synthase, and a detecting reagent capable of detecting the label;

(c) contacting the first antibody, the second labeled antibody, and the detecting reagent with the first body fluid sample;

(d) contacting the first antibody, the second labeled antibody, and the detecting reagent with the second body fluid sample; and,

(e) detecting the amount of and determining the concentration of human lipocalin-type prostaglandin D synthase in the normal subject sample to provide a reference value and detecting the amount of and determining the concentration of human lipocalin-type prostaglandin D synthase in the test subject sample, wherein an increased concentration of human lipocalin-type prostaglandin D synthase in the test subject sample compared to the reference value indicates that the test subject has a high probability of having had or being at risk of having an ischemic disorder.

Claims 19 and 20 are kit claim and read as follows:

19. A kit for detecting an ischemic disorder comprising two antibodies, a detecting reagent, and instructions, wherein each antibody has specific reactivity for a human lipocalin-type prostaglandin D synthase and the instructions set forth a method comprising the following steps:

(a) providing a first and a second body fluid sample, wherein the first sample is taken from a test subject from which an ischemic disorder is to be detected or predicted and the second sample is taken from a normal subject, and the body fluid sample is selected from the group consisting of a blood sample, a urine sample, a saliva sample and a semen sample;

(b) providing a first antibody and a second labeled antibody, wherein both the first and the second antibodies are capable of specifically binding to a human lipocalin-type prostaglandin D synthase, and a detecting reagent capable of detecting the label;

(c) contacting the first antibody, the second labeled antibody, and the detecting reagent with the first body fluid sample;

(d) contacting the first antibody, the second labeled antibody, and the detecting

reagent with the second body fluid sample; and,

(e) detecting the amount of and determining the concentration of human lipocalin-type prostaglandin D synthase in the normal subject sample to provide a reference value and detecting the amount of and determining the concentration of human lipocalin-type prostaglandin D synthase in the test subject sample, wherein an increased concentration of human lipocalin-type prostaglandin D synthase in the test subject sample compared to the reference value indicates that the test subject has a high probability of having had or being at risk of having an ischemic disorder.

20. A kit for detecting an ischemic disorder comprising two antibodies, a detecting reagent, and instructions, wherein each antibody has specific reactivity for a human lipocalin-type prostaglandin D synthase and the instructions set forth a method comprising the following steps:

(a) providing a body fluid sample from a normal subject, wherein the body fluid sample is selected from the group consisting of a blood sample, a urine sample, a saliva sample and a semen sample,

(b) providing a first antibody and a second labeled antibody, wherein both the first and the second antibodies are capable of specifically binding to a human lipocalin-type prostaglandin D synthase, and a detecting reagent capable of detecting the label;

(c) providing a reference value of the concentration of human lipocalin-type prostaglandin D synthase in the normal body fluid sample provided in step (a) using the first antibody, the second labeled antibody, and the detecting reagent;

(d) providing a test body fluid sample from a test subject from which an ischemic disorder is to be detected or predicted, wherein the body fluid is the same type of body fluid provided in (a);

(e) contacting the first antibody, the second labeled antibody, and the detecting reagent with the test subject body fluid sample;

(f) detecting the amount of and determining the concentration of human lipocalin-type prostaglandin D synthase in the normal subject sample to generate a reference value, wherein an increased concentration of human lipocalin-type prostaglandin D synthase in the test subject sample compared to the reference value indicates that the test subject has a high probability of having had or being at risk of having an ischemic disorder.

Applicants respectfully direct the Examiner's attention to the fact that the kits contain antibodies specific against human lipocalin-type prostaglandin D synthase and instructions for

performing the novel methods. Antibodies specific against human lipocalin-type prostaglandin D synthase are known. See Caymen Chemical at http://www.caymanchem.com/neptune/servlet/neptune/catalog/160003/template/Product.vm/a/z which sells 160003 Prostaglandin D Synthase (Lipocalin type) Polyclonal Antibody and states:

> Antigen: human lipocalin type PGD synthase amino acids 30-41 (VQPNFQPDKFLG)[1] · Host: rabbit · Cross-reactivity: (+) human PGD synthase; other species not tested · Application: WB; other applications not tested · Prostaglandin D synthase (PGD synthase) catalyzes the isomerization of PGH2 to produce PGD2. PGD2 induces sleep, regulates nociception, inhibits platelet aggregation, and acts as an allergic mediator. Two distinct types of PGD synthase have been identified, namely the lipocalin type enzyme (β-trace) and the hematopoietic enzyme.[2 3] Lipocalin type PGD synthase is localized in the central nervous system and male genital organs of various mammals and the human heart whereas the hematopoietic PGD synthase is widely distributed in the peripheral tissues and localized in the antigen-presenting cells, mast cells, and megakaryocytes.[2 4 5 6] The lipocalin-type PGD synthase has been identified as β-trace, which is a major protein in human cerebrospinal fluid.[3 7] Human lipocalin-type PGD synthase is a 190 amino acid protein with a calculated molecular weight of 21,016.[1]
>
> [1] Nagata, A., Suzuki, Y., Igarashi, M., et al. Human brain prostaglandin D synthase has been evolutionarily differentiated from lipophilic-ligand carrier proteins. Proc. Natl. Acad. Sci. USA 88, 4020-4024 (1991).
> [2] Urade, Y., Watanabe, K., and Hayaishi, O. Prostaglandin D, E, and F synthases. J. Lipid Mediators Cell Signalling 12, 257-273 (1995).
> [3] Toh, H., Kubodera, H., Nakajima, N., et al. Glutathione-independent prostaglandin D synthase as a lead molecule for designing new functional proteins. Protein Engineering 9, 1067-1082 (1996).
> [4] Tokugawa, Y., Kunishige, I., Kuboto, Y., et al. Lipocalin-type prostaglandin D synthase in human male reproductive organs and seminal plasma. Biol. Reprod. 58, 600-607 (1998).
> [5] Melegos, D.N., Diamandis, E.P., Oda, H., et al. Immunofluorometric assay of prostaglandin D synthase in human tissue extracts and fluids. Clin. Chem. 42, 1984-1991 (1996).
> [6] Kanaoka, Y., Fujimori, K., Kikuno, R., et al. Structure and chromosomal localization of human and mouse genes for hematopoietic prostaglandin D synthase. Eur. J. Biochem. 267, 3315-3322 (2000).
> [7] Zahn, M., Mäder, A., Schmidt, B., et al. Purification and N-terminal sequence of β-trace, a protein abundant in human cerebrospinal fluid. Neurosci. Lett. 154, 93-95 (1993)

As provided in the references above (see reference #5), antibodies against human prostaglandin D synthase (lipocalin type) were known a year before even the Japanese patent

application from which the PCT application was based from which the '827 patent was based. Clearly, human lipocalin-type prostaglandin D synthase was prior art and the fact that the kits contain instructions for conducting the novel and nonobvious method was sufficient for patentability.

Therefore, Applicants respectfully submit that the kit claims of the present invention as presented herein are novel and nonobvious and that the rejection under 35 U.S.C. 103(a) should properly be withdrawn.

Applicants have also added claims 15 and 16 as suggested by the Examiner. Claims 15 and 16 are dependent on the method claims, claims 1 and 8, and comprise using kits to perform the methods. Applicants respectfully submit that since the base claims of claims 15 and 16 were found allowable over the prior art, claims 15 and 16 should be allowed.

Request for an Interview

Applicants greatly appreciate the Examiner's assistance. Should there by any remaining issues after entry of the amendment and consideration of the remarks herein, Applicants respectfully request either an in-person interview or a telephonic interview with the Examiner.

CONCLUSION

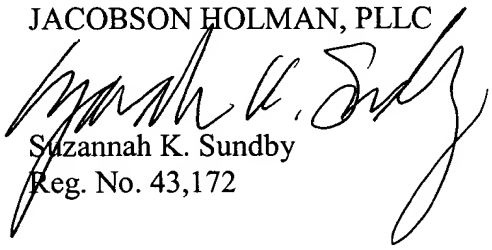
All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor are hereby

authorized to be charged to our Deposit Account No. **06-1358**, referencing Attorney Docket No. **P68884US0.**

Respectfully submitted,

JACOBSON HOLMAN, PLLC



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6. A kit comprising a vessel or vessels containing purified cytokine A and purified cytokine B.

7. An article of manufacture comprising a vial containing purified cytokine A and purified cytokine B, or, packaged together, a vial containing purified cytokine A and a vial containing purified cytokine B.

The "purified" limitation is included in the above claims to be certain that the claims are not interpreted as reading on, for example, a vial of serum that happens to contain the two cytokines.

ii. Known composition with a new use

If the invention is a new use for an old composition, merely saying that the composition is in a vessel within a kit will not lend patentability to the composition itself. However, claims to the method of use may not be all to which the applicant can aspire. Sometimes claims to a kit or article of manufacture containing the composition *labeled for use in the new method* have passed muster. Claims 8 and 9 illustrate two possibilities.

8. An article of manufacture comprising, packaged together:

a vessel containing enzyme A; and

instructions for use of enzyme A for the treatment of myocarditis in a method comprising (a) identifying a patient suspected of having myocarditis, and (b) administering an effective amount of enzyme A to the patient.